

Serial No.: 10/691,157

Confirmation No.: 6536

Filed: 22 October 2003

For: USE OF COLOSTRININ, CONSTITUENT PEPTIDES THEREOF, AND ANALOGS THEREOF AS
MODULATORS OF INTRACELLULAR SIGNALING MOLECULES

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

Listing of Claims

1. **(Currently Amended)** A method of modulating an intracellular signaling molecule in a cell, the method comprising contacting the cell with an effective amount of a modulator selected from the group consisting of colostrinin, a constituent peptide of colostrinin thereof, an active analog of a constituent peptide of colostrinin thereof, and combinations thereof, under conditions effective to accomplish at least one of the following:

reduce 4-hydroxynonenal (4HNE)-protein ~~4HNE-protein~~ adduct formation;

inhibit 4HNE-mediated glutathione depletion;

inhibit 4HNE-induced activation of p53 protein; or

inhibit 4HNE-induced activation of c-Jun NH2-terminal kinases;

wherein the constituent peptide of colostrinin is selected from the group consisting of

MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2),

DQPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4),

DLEMPVLPVEPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6),

VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO: 8);

wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent sequence identity to a constituent peptide of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLP (SEQ ID NO:4), DLEMPVLPVEPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPKLKVEVFPFP (SEQ ID NO:8); and

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further wherein the active analog accomplishes at least one of the following: reduces 4HNE-protein adduct formation; inhibits 4HNE-mediated glutathione depletion; inhibits 4HNE-induced activation of p53 protein; or inhibits 4HNE-induced activation of c-Jun NH2-terminal kinases.

2. (Original) The method of claim 1 wherein the cell is present in a cell culture, a tissue, an organ, or an organism.

3. (Original) The method of claim 1 wherein the cell is a mammalian cell.

4. (Original) The method of claim 3 wherein the cell is a human cell.

5. (Original) The method of claim 1 wherein the modulator is a constituent peptide of colostrinin.

6. (Currently Amended) The method of claim 5 wherein the modulator is selected from the group of MQPPPLP (SEQ ID NO:1), LQTPQPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLPFQVQS (SEQ ID NO:3), LFFFLPVVNVLP (SEQ ID NO:4), DLEMPVLPVEPFPPV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), LKPFPKLKVEVFPFP (SEQ ID NO:8), ~~VVMEV (SEQ ID NO:9), SEQP (SEQ ID NO:10), DKE (SEQ ID NO:11), FPPPK (SEQ ID NO:12), DSQPPV (SEQ ID NO:13), DPPPPQS (SEQ ID NO:14), SEEMP (SEQ ID NO:15), KYKLPQE (SEQ ID NO:16), VLPPNVG (SEQ ID NO:17), VYPFTGPIPN (SEQ ID NO:18), SLPQNILPL (SEQ ID NO:19), TQTPVVVPPF (SEQ ID NO:20), LQPEIMGVVKVETMVPK (SEQ ID NO:21), HKEMPPFKYPVEPFTESQ (SEQ ID NO:22), SLTLTDVEKLHLPLPLVQ (SEQ ID NO:23), SWMHQPP (SEQ ID NO:24), QPLPPTVMFP (SEQ ID NO:25), PQSVLS (SEQ ID NO:26), LSQPKVLPVPQKAVPQRDMPIQ (SEQ ID NO:27), AFLLYQE (SEQ ID NO:28), RGPFPILV (SEQ ID NO:29), ATFNRYQDDHGEELKSL (SEQ ID NO:30), VESYVPLFP~~

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~~(SEQ ID NO:31), FLLYQEPVLGPVR (SEQ ID NO:32), LNF (SEQ ID NO:33), and
MHQPPQPLPPTVMFP (SEQ ID NO:34);~~ and combinations thereof.

7. **(Currently Amended)** A method of down regulating the 4-hydroxynonenal (4HNE)-mediated oxidative damage associated with 4HNE-mediated lipid peroxidation in a cell, the method comprising contacting the cell with an effective amount of a modulator selected from the group consisting of colostrinin, a constituent peptide of colostrinin thereof, an active analog of a constituent peptide of colostrinin thereof, and combinations thereof[.,,];

wherein[[:]] the ~~active analog is an active analog of a constituent peptide of colostrinin is~~ selected from the group consisting of SEQ ID NO:1 through SEQ ID ~~NO:8 NO:34~~;

wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to a one or more constituent peptide[[:s]] of colostrinin selected from the group consisting of MQPPPLP (SEQ ID NO:1) LOTPOPLLQVMMEPQGD (SEQ ID NO:2), DQPPDVEKPDLOPFQVQS (SEQ ID NO:3), LFFFLPVGVLP (SEQ ID NO:4), DLEMPVLPVEPFV (SEQ ID NO:5), MPQNFYKLPQM (SEQ ID NO:6), VLEMKFPPPPQETVT (SEQ ID NO:7), and LKPFPCCKVEVFPFP (SEQ ID NO:8); and further wherein the active analog does not interfere with cellular uptake of redox-sensitive 2',7'-dihydro-dichlorofluorescein-diacetate;
and wherein 4HNE-mediated oxidative damage associated with lipid peroxidation in the cell is down regulated.

8-9. **(Cancel)**